

Attorney Docket No. 27110-701

**REMARKS**

This Amendment is in response to the Examiner's Office Action mailed on November 26, 2006 and furthermore in response to a telephone interview with the Examiner was initiated by Applicant on May 21, 2003. The Examiner's courtesy is appreciated. Applicants discussed the references cited by the Examiner in the final Office Action. The amendments and remarks herein are believed to reflect the interview.

Claims 12, 14, 15, 31, and 33-35 are withdrawn. Claims 2, 20, 52-54 are cancelled. Claims 1, 19, 46, 51 and 55 are currently amended. Claims 1, 3-11, 13, 16-19, 21-30, 32, 36-51 and 55 are now pending. Reconsideration is respectfully requested in view of the following remarks.

**I. Claim Objections**

Claims 1, 11, 19, 30, 51, and 52 were objected to on the basis that they recited species that were not specifically elected. Applicants believe that the amendments render this objection moot.

**II. Claim Rejections Under 35 U.S.C. 112, First Paragraph:**

The rejection under 35 U.S.C. 112, first paragraph, stands moot as a result of Applicants' amendment of claims.

**III. Claim Rejections Under 35 U.S.C. 102(b):**

The rejection under 35 U.S.C. 102 stands moot as a result of Applicants' amendment of claims.

**IV. Claims Rejections Under 35 U.S.C. 103(a):**

The Examiner rejected claims 1-11, 13, 16-30, 32, 36-51 and 55 under 35 U.S.C. 103(a) as being unpatentable over De La Fuente *et al.*, Hastie *et al.*, Rothschild *et al.* and Pierce Catalog & Handbook, 1994-1995. In particular, the Examiner stated that the above references render the claimed invention obvious by providing a reasonable expectation of success.

Applicants respectfully traverse Examiner's rejection under 35 U.S.C. 103(a) for the following reason.

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De La Fuente *et al.* and Hastie *et al.* disclose the use of sulfosuccinimidyl 6-biotinamido hexanoate (NHS-LC-Biotin) for the identification and isolation of lumen-exposed molecules but fail to teach the use of an impermeable cell-membrane reagent that is cleavable specifically under mild conditions. Examples of "mild conditions" include those disclosed on page 23 of the specification and any other conditions known by persons having ordinary skill in the art to cleave the cleavage without generating contaminants such as naturally biotinylated polypeptides and non-specifically bound polypeptides which are not eluted under mild conditions. Rothschild *et al.* provides allegedly a general description of heterobifunctional crosslinkers for use in detection and isolation of biomolecules but fails to teach or suggest the administration of reagents into a perfusable space. Pierce Catalog & Handbook teaches the use of cleavable NHS-SS-biotin for isolating proteins from a mixture of proteins but fails to teach the administration of any reagents into a perfusable space.

Consequently, none of the above references (independently or in combination with one another) teach, suggest or obviate the claimed invention wherein a cell membrane impermeable reagent having a cleavable chemical moiety capable of being cleaved under mild conditions is used for labeling, detecting or isolating lumen exposed molecules, especially tissue-specific or organ-specific molecules that are exposed on a luminal surface of a perfusable space. Such tissue-specific and organ-specific molecules may be present on one or more organs or tissues in the body. One advantage of using a cleavable moiety that can be cleaved under mild conditions is illustrated in Example 2, Figure 5, which shows protein profiles that were eluted using NHS-LC-biotin and NHS-SS-biotin. Lanes 1 and 3 illustrate proteins that were eluted using NHS-LC-biotin under harsh conditions and lanes 2 and 4 illustrate proteins that were eluted using NHS-SS-biotin under mild conditions. The two profiles are significantly different. Elution of molecules tagged with NHS-SS-biotin under mild conditions showed no staining over background, while elution under harsh conditions showed significant levels of background due to the presence of endogenously biotinylated proteins and other proteins that interact with the matrix (e.g., avidin beads).

As none of the above references (independently or in combination) teach or suggest the claimed invention, Applicants respectfully requests that the rejection under 35 U.S.C. §103(a) be withdrawn.


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CONCLUSION

In light of the remarks set forth above, Applicants believe that they are entitled to a letters patent. Applicants respectfully solicit the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner have any question, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

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